# **PCT**

# WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



#### INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

1) International Patent Classification 7:	A2	(11) International Publication Number: WO 00/61614					
C07K 14/00, C12P 21/06	(43) International Publication Date: 19 October 2000 (19.10.00)						
21) International Application Number: PCT/USC 22) International Filing Date: 6 April 2000 (C 30) Priority Data: 60/128,701 9 April 1999 (09.04.99) 60/142,821 8 July 1999 (08.07.99) 60/149,448 18 August 1999 (18.08.99) 60/164,751 12 November 1999 (12.11.99) 71) Applicant (for all designated States except US):	06.04.0 L L U 9) L HUMA	BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JF KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RL SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UC US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AN AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM GA, GN, GW, ML, MR, NE, SN, TD, TG).					
GENOME SCIENCES, INC. [US/US]; 9410 K Avenue, Rockville, MD 20850 (US).  72) Inventors; and 75) Inventors/Applicants (for US only): RUBEN, Ste [US/US]; 18528 Heritage Hills Drive, Olney, M (US). NI, Jian [CN/US]; 5502 Manorfield Road, R MD 20853 (US). KOMATSOULIS, George [US/U Garwood Street, Silver Spring, MD 20901 (US). Craig, A. [US/US]; 22400 Rolling Hill Road, Lay MD 20882 (US). SOPPET, Daniel, R. [US/US] Stillfield Place, Centreville, VA 22020 (US).  74) Agents: HOOVER, Kenley, K. et al.; Human Genome Inc., 9410 Key West Avenue, Rockville, MD 2085	even, 1 ID 208: Rockvill JS]; 95 ROSE vtonsvil]; 150:	Published  With declaration under Article 17(2)(a); without abstract title not checked by the International Searching Authority.  1. 2 e. 8 e. 6					
54) Title: UNCOUPLING PROTEINS							

### FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

			a - :	LS	Lesotho	SI	Slovenia
	Albania	ES	Spain	LT	Lithuania	SK	Slovakia
	Armenia	FI	Finland	LU	Luxembourg	SN	Senegal
r	Austria	FR	France	LV	Latvia	SZ	Swaziland
υ	Australia	GA	Gabon	MC	Monaco	TD	Chad
č	Azerbaijan	GB	United Kingdom	MD	Republic of Moldova	TG	Togo
4	Bosnia and Herzegovina	GE	Georgia	MG	Madagascar	TJ	Tajikistan
В	Barbados	GH	Ghana	MK	The former Yugoslav	TM	Turkmenistan
E	Belgium	GN	Guinea	MIK	Republic of Macedonia	TR	Turkey
F	Burkina Faso	GR	Greece	ML	Mali	TT	Trinidad and Tobago
G	Bulgaria	HU	Hungary	MN		UA	Ukraine
3J	Benin	IE	Ireland	MR	Mongolia Mauritania	UG	Uganda
BR	Brazil	IL	Israel	MW	Malawi	US	United States of America
BY	Belarus	IS	Iceland	MX	Marawi Mexico	UZ	Uzbekistan
CA	Canada	ľT	ltaly	NE.	-	VN	Viet Nam
CF	Central African Republic	JP	Japan		Niger	YU	Yugoslavia
CG	Congo	KE	Kenya	NL	Netherlands	zw	Zimbabwe
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	2**	Zimbaowe
CI	Côte d'Ivoire	KP	Democratic People's	NZ	New Zealand		
CM	Cameroon		Republic of Korea	PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

#### What Is Claimed Is:

- 1. An isolated nucleic acid molecule comprising a polynucleotide selected from the group consisting of:
- (a) the polynucleotide shown as SEQ ID NO:X or the polynucleotide encoded by a cDNA included in ATCC Deposit No:Z;
- (b) a polynucleotide encoding a biologically active polypeptide fragment of SEQ ID NO:Y or a biologically active polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No:Z;
- (c) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No:Z;
- (d) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(c), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.
- 2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide comprises a nucleotide sequence encoding a soluble polypeptide.
- 3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:Y or the polypeptide encoded by the cDNA sequence included in ATCC Deposit No:Z.

- 4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide comprises the entire nucleotide sequence of SEQ ID NO:X or a cDNA included in ATCC Deposit No:Z...
- 5. The isolated nucleic acid molecule of claim 2, wherein the polynucleotide is DNA.
- 6. The isolated nucleic acid molecule of claim 3, wherein the polynucleotide is RNA.
  - 7. A vector comprising the isolated nucleic acid molecule of claim 1.
  - A host cell comprising the vector of claim 7.
- 9. A recombinant host cell comprising the nucleic acid molecule of claim l operably limited to a heterologous regulating element which controls gene expression.
- 10. A method of producing a polypeptide comprising expressing the encoded polypeptide from the host cell of claim 9 and recovering said polypeptide.
- 11. An isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:
- (a) the polypeptide shown as SEQ ID NO:Y or the polypeptide encoded by the cDNA;

- (b) a polypeptide fragment of SEQ ID NO:Y or the polypeptide encoded by the cDNA;
- (c) a polypeptide epitope of SEQ ID NO:Y or the polypeptide encoded by the cDNA; and
  - (d) a variant of SEQ ID NO:Y.
- 12. The isolated polypeptide of claim 11, comprising a polypeptide having SEQ ID NO:Y.
- 13. An isolated antibody that binds specifically to the isolated polypeptide of claim 11.
- 14. A recombinant host cell that expresses the isolated polypeptide of claim 11.
  - 15. A method of making an isolated polypeptide comprising:
- (a) culturing the recombinant host cell of claim 14 under conditions such that said polypeptide is expressed; and
  - (b) recovering said polypeptide.
  - 16. The polypeptide produced by claim 15.
- 17. A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 11 or the polynucleotide of claim 1.

- 18. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:
- (a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and
- (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.
- 19. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:
- (a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and
- (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.
- 20. A method for identifying a binding partner to the polypeptide of claim 11 comprising:
  - (a) contacting the polypeptide of claim 11 with a binding partner; and
  - (b) determining whether the binding partner effects an activity of the polypeptide.
  - 21. A method of screening for molecules which modify activities of the polypeptide of claim 11 comprising:
  - (a) contacting said polypeptide with a compound suspected of having agonist or antagonist activity; and
    - (a) assaying for activity of said polypeptide.

ì

```
<110> Human Genome Sciences, Inc.
<120> Uncoupling Proteins
<130> PT009PCT
<140> Unassigned
<141> 2000-04-06
<150> 60/142,821
<151> 1999-07-08
<150> 60/149,448
<151> 1999-08-18
<150> 60/164,751
<151> 1999-11-12
<150> 60/128,701
<151> 1999-04-09
<160> 66
<170> PatentIn Ver. 2.0
<210> 1
<211> 733
<212> DNA
<213> Homo sapiens
<400> 1
gggatccgga gcccaaatct tctgacaaaa ctcacacatg cccaccgtgc ccagcacctg
                                                                          60
aattegaggg tgeaecgtea gtetteetet teeecceaaa acceaaggae acceteatga
                                                                         120
totocoggac tootgaggto acatgogtgg tggtggacgt aagccacgaa gaccotgagg
                                                                         180
tcaagttcaa ctggtacgtg gacggcgtgg aggtgcataa tgccaagaca aagccgcggg
                                                                         240
aggageagta caacageacg taccgtgtgg teagegteet caccgteetg caccaggact
                                                                         300
ggctgaatgg caaggagtac aagtgcaagg tctccaacaa agccctccca acccccatcg
                                                                         360
agaaaaccat ctccaaagcc aaagggcagc cccgagaacc acaggtgtac accctgcccc
                                                                         420
cateceggga tgagetgace aagaaceagg teageetgae etgeetggte aaaggettet
                                                                         480
 atocaagoga catogoogtg gagtgggaga gcaatgggca gccggagaac aactacaaga
                                                                         540
 coacgectee egtgetggae tecgaegget cettetteet etacageaag eteacegtgg
                                                                         600
 acaagagcag gtggcagcag gggaacgtct tctcatgctc cgtgatgcat gaggctctgc
                                                                         660
 acaaccacta cacgcagaag agecteteec tgteteeggg taaatgagtg egaeggeege
                                                                         720
                                                                         733
 gactctagag gat
```

<210> 2 <211> 1560

<212> DNA

DNIO ---- 004

2

### <213> Homo sapiens

<400> 2 ctaggtgcgc tgcgagcgcg		descadedd	cggagccggt	atgggcccgc	60
ctaggtgcgc tgcgagcgcg	egeggaeege	cadcctadad	ccaggactga	agcttcaaga	120
ctaggtgcgc tgcgagcgcc ctggccctgg gcgccgcgcc	gcacgagcac	cagootagas	aatogtggcc	tcaggcaccg	180
ctggccctgg gcgccgcgcc tggctgacca ggaccctgcg	ggcatcagcc	coctocago	ggtgaaggtt	cgcctgcagt	240
tggctgacca ggaccctgcg gggctgtggt tacctctctc	ttdatgacac	tacattacta	cagactgtgg	agectetect	300
gggctgtggt tacctctctc ctcagcggcc ctccatggcc	agcgagctga	startatect	ggageetetg	tacctgtgcc	360
ctcagcggcc ctccatggcc ataccaaatg gaagtgcctc	ctgtattgca	acggcgccctac	ccacttcact	ggcaccatgg	420
ataccaaatg gaagtgcctc caaatggtgc ccgctgtgcc	acctggtttc	aagaccccac	cctctggage	ggcctccccg	480
caaatggtgc ccgctgtgcc atgccttcgt gaagatcgtg	aggcacgagg	gcaccaggue	cactgcctat	gaccaactga	540
ccaccctggt gatgactgtg	ccagctaccg	ctgacctcta	cocacccatg	gtggctggcg	600
aggeetteet gtgtggtega	geeetgacee	transcent	ggagettatg	cggacaaagc	660
cgctggcccg cctgggcacc	gegaetgega	taagtaccta	tottcgaact	gcagtggctc	720
tgcaggctca gcatgtgtcg	taccgggage	addacccac	tgcccttcga	gatgtgccct	780
agggtggctg gcgctcactg tctcagccct gtactggttc	tggctgggct	tagtgaagag	ctggctcaat	gggctcaggc	840
totcagocot gtactggtto cgaaggacca gacttotgtg	aactatgage	ttataactaa	tggcatctca	gggacggtgg	900
cgaaggacca gacttctgtg ctgcagtgct gactctaccc	+++aacataa	taaagaccca	acgccaggtc	gctctgggag	960
ctgcagtgct gactctaccc cgatggaggc tgtgagagtg	titigacgtgg	atgtggactc	cacctggctg	ctgctgcgga	1020
cgatggaggc tgtgagagtg ggatccgggc cgagtcgggc	aacccccgc	tctttgcagg	cttccttcct	cggatcatca	1080
ggatecggge egagteggge aggetgeece etectgtgee	accangggas	gcacctatga	gttcggcaaa	agcttcttcc	1140
aggetgeece etectgtgee agaggetgaa eeaggaeegg	. cttctgggg	gctgaaaggg	gcaaggaggo	aaggaccccg	1200
agaggetgaa ceaggaeegg teteteecae ggatggggae	· suudcadgg	gagacccago	caagtgcctt	ttcctcagca	1260
teteteecae ggatgggag ctgagggagg gggettgttt	- ccetteect	ccggcgacaa	gctccagggc	agggetgtee	1320
ctgagggagg gggcttgttt ctctgggcgg cccagcactt	cctcagacac	aacttcttcc	tgctgctcca	gtogtgggga	1380
ctctgggcgg cccagcacti tcatcactta cccaccccc	aagttcaag	a ccaaatctto	cagetgeece	: cttcgtgttt	1440
teatcactta cccaccccccccccccccccccccccccc	gacatgtete	c caggaaccaa	a gaagccctca	gcctggtgta	1500
ccctgtgttt gctgtagctg gtctccctga cccttgtta	a tteettaag	t ctaaagatga	a tgaaaaaaa	aaaaaaaaaa	1560
gtctccctga cccttgtta					

<210> 3 <211> 1566 <212> DNA <213> Homo sapiens

tegacecacg egteegegga egegtgggeg gaegegtggg tegeggagee gggeegeace 60 egecgageeg tettgataet gatggaeatt gtgtgggeea gaggeaggga tggttggeta 120 tgaccccaaa ccagatggca ggaataacac caagttccag gtggcagtgg ctgggtctgt 180 gtctggactt gttactcggg cgctgatcag tcccttcgac gtcatcaaga tccgtttcca 240 getteageat gagegeetgt etegeagtga ecceagegea aagtaceatg geateeteea 300 ggcctctagg cagattctgc aggaggaggg tccgacagct ttctggaaag gacacgtccc 360 ageteagatt etetecatag getatggage tgtecaatte ttgteatttg aaatgetgae 420 ggagetggte cacagaggea gegtgtacga egecegggaa ttetcagtge actttgtatg 480 tggtggcctg gctgcctgta tggccaccct cactgtgcac cccgtggatg ttctgcgcac 540 cogetttgca getcagggtg agcccaaggt ctataatacg etgegecacg ecgtggggac 600 catgtatagg agcgaaggcc cccaggtttt ctacaaaggc ttggctccca ccttgatcgc 660 catcttcccc tacgecgggc tgcagttctc ttgctacagc tecttgaagc acctgtacaa 720 gtgggccata ccagccgaag gaaagaaaaa tgagaacctc caaaacctgc tttgtggcag 780 tggagetggt gtcatcagea agaecetgae atateegetg gaectettea agaagegget 840

			gangtoctco	taacctcgtc	ccctctcage	360
aggcccctgc	tgtcccccca	ectgergger	gagetetee	anct aggcac	tacatageet	420
						480
						540
	DEDDOOR	COCTATIALC		900		
						600
catcttccag	Cactttttt	-hearetted	tatatactas	gagcaaccag	accttccatg	660
tgctcaccca	agtgctagct	Cigcaccicg	tgtctgctga	gatagatga	acaagcaacg	720
						780
						840
						900
						960
cctgcgtccc	togggeacer	999000000	Cuacaannan	tccgacgggg	cggatgctgc gtgctctgtg	1020
ggccgcggtt	cctccttagg	geetteteet	cyacaaggag	gaagggagt	atactetata	1080
						1140
gagget geaa	tcaataaatg	ccgggagctg	ccaaaaaaaa	aaaaaaaaa	aaaaaaaaa	1178
9999009000	aaaaaaaaaa	aaaaaaaaa	aaaaaaa			1170
aaaaaaaaa						

<210> 20 <211> 351 <212> PRT <213> Homo sapiens

Met Ala Asp Gln Asp Pro Ala Gly Ile Ser Pro Leu Gln Gln Met Val

Ala Ser Gly Thr Gly Ala Val Val Thr Ser Leu Phe Met Thr Pro Leu 25

Asp Val Val Lys Val Arg Leu Gln Ser Gln Arg Pro Ser Met Ala Ser

Glu Leu Met Pro Ser Ser Arg Leu Trp Ser Leu Ser Tyr Thr Lys Trp 55

Lys Cys Leu Leu Tyr Cys Asn Gly Val Leu Glu Pro Leu Tyr Leu Cys

Pro Asn Gly Ala Arg Cys Ala Thr Trp Phe Gln Asp Pro Thr Arg Phe

Thr Gly Thr Met Asp Ala Phe Val Lys Ile Val Arg His Glu Gly Thr 105

Arg Thr Leu Trp Ser Gly Leu Pro Ala Thr Leu Val Met Thr Val Pro 120

Ala Thr Ala Ile Tyr Phe Thr Ala Tyr Asp Gln Leu Lys Ala Phe Leu 135 130

Cys Gly Arg Ala Leu Thr Ser Asp Leu Tyr Ala Pro Met Val Ala Gly

16

145					150					155					160
	Leu	Ala	Arg	Leu 165	Gly	Thr	Val	Thr	Val 170	Ile	Ser	Pro	Leu	Glu 175	Leu
Met	Arg	Thr	Lys 180	Leu	Gln	Ala	Gln	ніs 185	Val	Ser	Tyr	Arg	Glu 190	Leu	Gly
		195					200				Trp				
	210					215					Pro 220				
225					230					233	Leu				
				245					250		Val				
			260					200			Phe				
		275	5				280								Asn
	290	0				295					500				Ala
30	5				310	)				31-	,				320
				325	ō				331	,					
Ly	s Se	r Ph	e Ph		n Arq	g Le	ı Asr	34	n As) 5	p Ar	g Le	ı Lev	35	y Gl	Y
<2 <2	210> 211> 212> 213>	320 PRT	sap	oiens											
< ·	400> et Va	21 al G	ly Ty	r As	p Pr 5	o Ly	s Pr	o As	p Gl 1	y Ar .0	g As	n As	n Th	r Ly 1	s Phe
G	ln V	al A		al Al 20	a Gl	y Se	r Va	1 Se	er G] 25	.y L∈	eu Va	.l Th	r Ai	g A] 30	La Leu